

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
14 February 2002 (14.02.2002)

PCT

(10) International Publication Number  
**WO 02112277 A3**

(51) International Patent Classification: **C12N 15/62.**  
C07K 14/00.C12N 15/10

(21) International Application Number: PCT/GB01/03508

(22) International Filing Date: 3 August 2001 (03.08.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
0019362.3 7 August 2000 (07.08.2000) GB  
0102678.0 2 February 2001 (02.02.2001) GB

(71) Applicant (for all designated States except US): **DIVERSYSLIMITED [GB/GB]**; 20 Park Crescent. London WIN 4AL (GB).

(72) Inventors; and  
(75) Inventors/Applicants (for US only): **RIECHMANN, Lutz [DE/GB]**; MRC Laboratory of Molecular Biology. Hills Road. Cambridge CB2 2QH (GB). **WINTER, Greg [GB/GB]**; MRC Laboratory of Molecular Biology. Hills Road, Cambridge CB2 2QH (GB).

(74) Agents: **MASCHIO, Antonio et al.**; D Young & Co., 21 New Fetter Lane. London EC4A 1DA (GB).

(81) Designated States (*national*): AE. AG. AL. AM. AT. AU. AZ. BA. BB. BG. BR. BY. BZ. CA. CH. CN. CO. CR. CU. CZ. DE. DK. DM. DZ. EC. EE. ES. FI. GB. GD. GE. GH. GM. HR. HU. ID. IL. IN. IS. JP. KE. KG. KP. KR. KZ. LC. LK. LR. LS. LT. LU. LV. MA. MD. MG. MK. MN. MW. MX. MZ. NO. NZ. PL. PT. RO. RU. SD. SE. SG. SI. SK. SL. TJ. TM. TR. TT. TZ. UA. UG. US. UZ. VN. YU. ZA. ZW.

(84) Designated States (*regional*): ARIPO patent (GH. GM. KE. LS. MW. MZ. SD. SL. SZ. TZ. UG. ZW), Eurasian patent (AM. AZ. BY. KG. KZ. MD. RU. TJ. TM), European patent (AT. BE. CH. CY. DE. DK. ES. FI. FR. GH. GR. IE. IT. LU. MC. NL. PT. SE. TR), OAPI patent (BF. BJ. CF. CG. CI. CM. GA. GN. GQ. GW. ML. MR. NE. SN. TD. TG).

**Declaration under Rule 4.17:**

— of inventorship (Rule 4.17(iv)) for US only

**Published:**

— with international search report

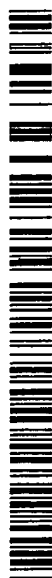
(88) Date of publication of the international search report:  
30 May 2002

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: HYBKID COMBINATORIAL PROTEINS MADE FROM RESHUFFLING OF DIFFERENTLY FOLDED DOMAINS

(57) Abstract: The present invention relates to a chimaeric folded protein domain comprising two or more sequence segments from parent amino acid sequences that are not homologous, wherein each of said sequence segments, in isolation, shows no significant folding at the melting temperature of the chimaeric protein; as well as to methods for the selection of such domains; and to a chimaeric folded protein domain comprising two or more sequence segments which share common sequences or sequences from common regions in the protein fold of their parent amino acid sequences, wherein, in isolation, each said sequence segment shows no significant folding at the melting temperature of the chimaeric protein; as well as to methods for the selection of such domains. The invention specifically relates to the application of said chimaeric protein domains for use in vaccination, wherein said chimaeric protein domains display conformational B cell epitopes of at least one of its parent amino acid sequences.

WO /12 77 A3



# INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 01/03508

## CLASSIFICATION OF SUBJECT MATTER

PC 7 C12N15/62 C07K14/00 C12N15/10

According to International Patent Classification (IPC) or to both national classification and IPC

## I. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

PC 7 C12N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data, WPI Data

## II. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication where appropriate, of the relevant passages	Relevant to claim No
X	WO 95 21914 A (PASTEUR MERIEUX SERUMS ET VACCINS) 17 August 1995 (1995-08-17) the whole document ---	31-37, 72-78
X	WO 97 32017 A (MORPHOSIS GMBH) 4 September 1997 (1997-09-04) the whole document ---	31-37, 72-78
A	WO 99 58655 A (MEDICAL RESEARCH COUNCIL) 18 November 1999 (1999-11-18) the whole document --- -/--	31-37, 72-78

☒ Further documents are listed in the continuation of box C

☐ Patent family members are listed in annex

### \* Special categories of cited documents

- 'A' document defining the general state of the art which is not considered to be of particular relevance
- 'E' earlier document but published on or after the international filing date
- 'L' document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- 'O' document referring to an oral disclosure, use, exhibition or other means
- 'P' document published prior to the international filing date but later than the priority date claimed

- 'T' later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- 'X' document of particular relevance the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- 'Y' document of particular relevance the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents such combination being obvious to a person skilled in the art
- '&' document member of the same patent family

Date of the actual completion of the international search

7 March 2002

Date of mailing of the international search report

15/03/2002

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Masturzo, P

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 01/03508

:(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	P J O'BRIEN & D HERSCHLAG: "Catalytic promiscuity and the evolution of new enzymatic activity" CHEMISTRY AND BIOLOGY, vol. 8, April 1999 (1999-04), pages R91-R105, XP000993553 CURRENT BIOLOGY, LONDON, GB ISSN: 1074-5521 the whole document ---	1-83
X	K-P HOPFNER ET AL.: "New enzyme lineages by subdomain shuffling" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA., vol. 95, August 1998 (1998-08), pages 9813-9818, XP002103693 NATIONAL ACADEMY OF SCIENCE. WASHINGTON., US ISSN: 0027-8424 the whole document ---	1-30
X	M FLAJOLET ET AL.: "A genomic approach of the hepatitis C virus generates a protein interaction map" GENE., vol. 242, no. 2, January 2000 (2000-01), pages 369-379, XP002178862 ELSEVIER BIOMEDICAL PRESS. AMSTERDAM., NL ISSN: 0378-1119 the whole document ---	1-30
A	M OSTERMEIER ET AL.: "Combinatorial protein engineering by incremental truncation" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA., vol. 96, March 1999 (1999-03), pages 3562-3567, XP002178863 NATIONAL ACADEMY OF SCIENCE. WASHINGTON., US ISSN: 0027-8424 cited in the application the whole document ---	1-30
X	M M ALTAMIRANO ET AL.: "Directed evolution of new catalytic activity using the alpha-beta-barrel scaffold" NATURE., vol. 403, 10 February 2000 (2000-02-10), pages 617-622, XP002178864 MACMILLAN MAGAZINES., US ISSN: 0028-0836 cited in the application the whole document --- -/--	1-30

# INT' NATIONAL SEARCH REPORT

International Application No

PCT/GB 01/03508

..(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
A	<p>A CRAMERI ET AL.: "DNA shuffling of a family of genes from diverse species accelerates directed evolution"</p> <p>NATURE.,</p> <p>vol. 391, 15 January 1998 (1998-01-15),</p> <p>pages 288-291, XP002178865</p> <p>MACMILLAN MAGAZINES., US</p> <p>ISSN: 0028-0836</p> <p>cited in the application</p> <p>the whole document</p> <p>---</p>	1-30
P,X	<p>L RIECHMANN &amp; G WINTER: "Novel folded protein domains generated by combinatorial shuffling of polypeptide segments"</p> <p>PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA.,</p> <p>vol. 97, no. 18,</p> <p>29 August 2000 (2000-08-29), pages</p> <p>10068-10073, XP002178866</p> <p>NATIONAL ACADEMY OF SCIENCE. WASHINGTON.,</p> <p>US</p> <p>ISSN: 0027-8424</p> <p>the whole document</p> <p>---</p>	1-83
P,X	<p>WO 01 42432 A (MRC)</p> <p>14 June 2001 (2001-06-14)</p> <p>the whole document</p> <p>-----</p>	1-30

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 9521914	A	17-08-1995	FR	2715940 A1	11-08-1995
			AU	1666895 A	29-08-1995
			CA	2183079 A1	17-08-1995
			EP	0742821 A1	20-11-1996
			WO	9521914 A1	17-08-1995
			JP	9509055 T	16-09-1997
WO 9732017	A	04-09-1997	WO	9732017 A1	04-09-1997
			EP	0883686 A1	16-12-1998
			JP	2000505306 T	09-05-2000
WO 9958655	A	18-11-1999	AU	3941399 A	29-11-1999
			EP	1078051 A2	28-02-2001
			GB	2361237 A	17-10-2001
			WO	9958655 A2	18-11-1999
			NO	20005628 A	12-01-2001
WO 0142432	A	14-06-2001	AU	1720501 A	18-06-2001
			WO	0142432 A2	14-06-2001
			GB	2358633 A	01-08-2001

THIS PAGE BLANK (4-1)